Human embryonic stem cells as models for aneuploid chromosomal syndromes.

Journal: Stem Cells

Publication Year: 2010

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PubMed link: 20641042

Funding Grants: Generation of Pluripotent Cell Lines from Human Embryos

Public Summary:
This publication describes the derivation of human embryonic stem cell lines from blastocysts diagnosed with aneuploidy following pre-implantation genetic screening. These human embryonic stem cell lines serve as new models to understand genetic disorders such as Patau Syndrome and Turner syndrome.

Scientific Abstract:
Syndromes caused by chromosomal aneuploidies are widely recognized genetic disorders in humans and often lead to spontaneous miscarriage. Preimplantation genetic screening is used to detect chromosomal aneuploidies in early embryos. Our aim was to derive aneuploid human embryonic stem cell (hESC) lines that may serve as models for human syndromes caused by aneuploidies. We have established 25 hESC lines from blastocysts diagnosed as aneuploid on day 3 of their in vitro development. The hESC lines exhibited morphology and expressed markers typical of hESCs. They demonstrated long-term proliferation capacity and pluripotent differentiation. Karyotype analysis revealed that two-third of the cell lines carry a normal euploid karyotype, while one-third remained aneuploid throughout the derivation, resulting in eight hESC lines carrying either trisomy 13 (Patau syndrome), 16, 17, 21 (Down syndrome), X (Triple X syndrome), or monosomy X (Turner syndrome). On the basis of the level of single nucleotide polymorphism heterozygosity in the aneuploid chromosomes, we determined whether the aneuploidy originated from meiotic or mitotic chromosomal nondisjunction. Gene expression profiles of the trisomic cell lines suggested that all three chromosomes are actively transcribed. Our analysis allowed us to determine which tissues are most affected by the presence of a third copy of either chromosome 13, 16, 17 or 21 and highlighted the effects of trisomies on embryonic development. The results presented here suggest that aneuploid embryos can serve as an alternative source for either normal euploid or aneuploid hESC lines, which represent an invaluable tool to study developmental aspects of chromosomal abnormalities in humans.